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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,206	05/03/2001	Philip Guy	82402-3801	9235
7590	03/15/2004		EXAMINER	
Ade & Company 1700 360 Main Street Winnipeg Manitoba, R3C 3Z3 CANADA			KALLIS, RUSSELL	
			ART UNIT	PAPER NUMBER
			1638	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/720,206

Applicant(s)

GUY ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12/24/2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 28-38 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 28-38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 December 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 3/7/2001.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Continued Prosecution Application***

The request for a continued prosecution application (CPA) under 37 CFR 1.53(d) filed on 12/24/2004 is acknowledged. 37 CFR 1.53(d)(1) was amended to provide that the CPA must be for a design patent and the prior application of the CPA must be a design application that is complete as defined by 37 CFR 1.51(b). See *Elimination of Continued Prosecution Application Practice as to Utility and Plant Patent Applications*, final rule, 68 *Fed. Reg.* 32376 (May 30, 2003), 1271 *Off. Gaz. Pat. Office* 143 (June 24, 2003). Since a CPA of this application is not permitted under 37 CFR 1.53(d)(1), the improper request for a CPA is being treated as a request for continued examination of this application under 37 CFR 1.114.

### ***Specification***

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973). The attempt to incorporate subject matter into this application by reference to Duff *et al.*, 1997, *Journal of Biological Chemistry*; 272, pp. 16746-16752, on page 2 of the specification, that teaches barley nonsymbiotic hemoglobins is improper. The stated reference does not contain the barley nonsymbiotic hemoglobin sequence.

Claims 28-38 are pending. Claims 28-38 are examined.

***Claim Rejections - 35 USC § 112***

Claims 28-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method of improving the agronomic properties of any plant by increasing cellular levels of any nonsymbiotic plant hemoglobin; a method of selecting or rejecting a seed based upon the levels of nonsymbiotic plant hemoglobin protein expression in a seed; and a method for determining seed germination by measuring nonsymbiotic plant hemoglobin levels in a seed.

Applicants do not describe any nonsymbiotic plant hemoglobins or any polynucleotide sequences that encode a nonsymbiotic plant hemoglobin, required to practice the claimed invention.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of

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nonsymbiotic plant hemoglobins within the scope of the claimed genus of nonsymbiotic plant hemoglobins. Applicants do not provide a written description of any nonsymbiotic plant hemoglobin. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of nonsymbiotic plant hemoglobins. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary structural elements essential for any nonsymbiotic plant hemoglobin activity, it remains unclear what features identify a nonsymbiotic plant hemoglobin. Since the genus of nonsymbiotic plant hemoglobins has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Sequences that have nonsymbiotic plant hemoglobin activity encompass naturally occurring allelic variants, mutants of nonsymbiotic plant hemoglobin, as well as sequences encoding proteins having no known nonsymbiotic plant hemoglobin activity, of which Applicant is not in possession. Accordingly, the specification fails to provide an adequate written description to support the genus of nonsymbiotic plant hemoglobin as set forth in the claims.

(See Written Description guidelines published in Federal Register/Vol. 66, No.4/Friday, January 5, 2001/Notices: p.1099-1111).

Claims 28-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists

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a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are broadly drawn to a method of improving the agronomic properties of a plant by increasing cellular levels of a nonsymbiotic plant hemoglobin; a method of selecting or rejecting a seed based upon the levels of nonsymbiotic plant hemoglobin expression in a seed; and a method for determining seed germination by measuring hemoglobin levels in a seed.

Applicant teaches expression of barley nonsymbiotic plant hemoglobin in transformed maize cells (Example III, page 10); measurement of hemoglobin protein in transformed maize cells (Example IV); increased energy status (i.e. increase in total adenylate and increases in ATP levels) in maize cells transformed with barley nonsymbiotic hemoglobin (Example VI, page 12 lines 21-25); increased oxygen uptake in transformed cells (Example VIII); faster recovery from anoxic shock in maize cells expressing barley hemoglobin (Example IX); and hemoglobin expression during germination of barley seeds (Example X). Applicant does not teach the improvement of any agronomic trait in any plant or any method for selecting or rejecting seeds based upon hemoglobin expression.

Engineering or breeding increases in hemoglobin levels in a plant is unpredictable because there are unknown unlinked genes directly related to acquiring the desired phenotype (Goodenough U., Genetics; 1978, 2<sup>nd</sup> ed., Holt, Rinehart and Winston; pages 771-772). Further,

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although plant nonsymbiotic hemoglobins have been observed in root and specific seed tissues under stress or during germination their function in plant metabolism is not entirely clear, and thus the affect upon plant metabolism from the expression of hemoglobins in plant tissue not normally expressing nonsymbiotic plant hemoglobins is unknown and therefore unpredictable (Dordas C. *et al.*, Annals of Botany, 2003, Vol. 91; pages 173-178; see page 173 column 1 3<sup>rd</sup> paragraph to column 2, line 6; page 173 column 2, see Historical Overview, lines 13-17; page 175 column 2 lines 1-9).

In addition, the isolation of any DNA sequences encoding nonsymbiotic plant hemoglobin from any species introduces an element of unpredictability. The limitation is introduced in finding homologous regions that would adequately enable either PCR amplification or southern hybridization and would entail using either degenerate primers or probes with limited sequence identity. Thus the screen for DNA sequences encoding nonsymbiotic plant hemoglobin from any species sequences would isolate many genes other than those of interest. The inherent unpredictability in isolation of a homologous DNA sequence encoding the same protein activity is illustrated in an example where a small number of changes to the coding region for a strict desaturase resulted in an enzyme with a hydroxylase activity and that a small number of changes to the coding region of a desaturase could account for functional divergence seen across a range of enzymes involved in fatty acid metabolism that have different specific activities (Broun P. *et al.* Science, Vol. 282; 13 November 1998, pp. 1315-1317; Abstract lines 4-6 and p. 1317 column 1, lines 37-56).

Based upon Applicant's limited guidance in the instant specification undue trial and error experimentation would be required by one of skill in the art to isolate and screen a multitude of

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non-exemplified DNA sequences encoding a plant nonsymbiotic hemoglobin and test for increases in cellular levels of hemoglobin in a plant either by breeding or by transformation of a myriad of non-exemplified plant species and to test for any number of improved agronomic properties in a plant having increased cellular levels of a plant nonsymbiotic hemoglobin, and to select or reject a seed based upon non-exemplified hemoglobin levels. Further, the specification is not enabling for the use of any hemoglobin because Applicant has not taught how to use any hemoglobin in a whole plant or whether all tissues would tolerate increases in the cellular levels of hemoglobin without compromising other essential cellular activities. Moreover, the specification does not provide guidance for any method other than plant transformation as a way of increasing cellular levels of nonsymbiotic plant hemoglobin.

Given the unpredictability in isolating DNA sequences encoding nonsymbiotic plant hemoglobin from any species or which plant tissue would allow for increased cellular levels of nonsymbiotic hemoglobin or which agronomic properties would be increased and how that would be determined and what levels of hemoglobin in a germinating seed would enable one of skill in the art to either reject or select a seed for breeding purposes; the breadth of claims encompassing any levels of increases of hemoglobin in any plant in any plant tissue during any time in plant development or any levels of hemoglobin expressed in a germinating seed, or any number of improved agronomic properties; the lack of guidance in the examples of the specification or the prior art; and the undue trial and error experimentation required to practice the claimed invention, the invention is not enabled.



***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 28-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Taylor, E. *et al.* Plant Molecular Biology, 1994; Vol. 24, pp. 853-862 taken with the evidence of Andersson C. *et al.* PNAS, June 1996; pages 5682-5687 ; see page 5686, column 2.

Taylor teaches providing increased levels of nonsymbiotic plant hemoglobin expression in root cells of water stressed barley and maize, i.e. growing the plant under stressful conditions, on page 859 column 2 to page 860 column 1; and because the reference teaches the method steps required for improving agronomic properties and since it is presumed the claimed effects are an inherent result of the method steps absent any evidence to the contrary; the improved agronomic properties of germination, seedling vigor, reduced cellular levels of fermentation products, increased oxygen uptake and increased tolerance to hypoxic conditions of Claims 30-34 are inherently taught. Thus, The reference teaches all the limitations of Claims 28-34.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 28-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taylor, E. *et al.*, Plant Molecular Biology, 1994; Vol. 24, pp. 853-862 in view of Hartl D. *et al.*, Genetics: Analysis of Genes and Genomes; 5<sup>th</sup> Ed., Jones and Bartlett Publishers; see page 766.

The claims are broadly drawn to a method of improving agronomic properties of a plant by providing increased cellular levels of nonsymbiotic plant hemoglobin expression, i.e. growing the plant under stressful conditions; and a method selecting seeds for breeding by providing a seed line, growing the seed, isolating extract from the seed, measuring levels of nonsymbiotic plant hemoglobin expression, and selecting or rejecting the seed for further breeding based on the hemoglobin levels; and a method of determining if a seed is germinating by measuring hemoglobin expression levels.

The teachings of Taylor E. *et al.* are discussed supra.

Taylor further teaches measuring levels of expression of nonsymbiotic plant hemoglobin in excised aleurone layers of barley seed imbibed for 3 days and in excised aleurone layers of barley seed incubated under low oxygen levels (page 855, column 2 and page 859, figure 4a).

Taylor does not teach selection or rejection of a seed based upon hemoglobin levels.

Hartl teaches artificial selection and heritability of a quantitative trait.

It would have been obvious at the time of Applicant's invention to modify the invention of Taylor to include a method of artificial selection wherein hemoglobin expression levels are positively correlated with seed germination. One of skill in the art would have been motivated by the teachings of Taylor that since nonsymbiotic plant hemoglobins maintain energy levels and help plant cells cope with stress they are valuable materials for genetic engineering of plants for improved agronomic properties and the knowledge common in the art that traits can be selected

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for by means of artificial selection, and that one would have had a reasonable expectation of success in measuring nonsymbiotic hemoglobin levels in plants.

All claims are rejected.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.  
March 3, 2004

A handwritten signature in black ink, appearing to read "Amy Nelson", with a stylized flourish at the end.

**AMY J. NELSON, PH.D**  
**SUPERVISORY PATENT EXAMINER**  
**TECHNOLOGY CENTER 1600**